We claim:

1. A method of determining the presence of an inflammatory disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 protein present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 protein with a predetermined standard;

wherein a difference in the amount of OP-1 protein present in said sample and the predetermined standard is indicative of the presence of inflammatory disease.

2. A method of determining the presence of an inflammatory disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 mRNA present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 mRNA with a predetermined standard;

wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined standard is indicative of the presence of inflammatory disease.

3. A method for determining the clinical severity of an inflammatory disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 protein present in a joint tissue sample; and

(b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 protein present in joint tissue samples obtained from members of a population having said inflammatory disease with the clinical severity of said disease,

thereby to determine the clinical severity of the inflammatory disease in said patient.

4. A method for determining the clinical severity of an inflammatory disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 mRNA present in a joint tissue sample; and

(b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 mRNA present in joint tissue samples obtained from members of a population having said inflammatory disease with the clinical severity of said disease,

thereby to determine the clinical severity of the inflammatory disease in said patient.

5. The method of any one of claims 1-4, wherein the joint tissue sample comprises a tissue selected from the group consisting of cartilage, ligament, meniscus, tendon, synovium, synovial fluid and intervertebral disc tissue.

6. The method of any one of claims 1-4, wherein the joint tissue sample comprises synovial fluid.

7. The method of claim 1 or 3, wherein the step of determining an amount of OP-1 protein present in the joint tissue sample comprises performing an enzyme-linked immunosorbent assay (ELISA).

8. The method of any one of claims 1-4, wherein the inflammatory disease is selected from the group consisting of rheumatoid arthritis, lupus erythematosus, gout, fibromyalgia syndrome, polymyalgia rheumatica, psoriasis, bacterial infection, viral infection and fungal infection.

9. A method of determining the presence of an age-related tissue disorder in a patient, the method comprising the steps of;

(a) determining an amount of OP-1 protein present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 protein with a predetermined standard,

wherein a difference in the amount of OP-1 protein present in said sample and the predetermined standard is indicative of an age-related tissue disorder.

10. A method of determining the presence of an age-related tissue disorder in a patient, the method comprising the steps of;

(a) determining an amount of OP-1 mRNA present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 mRNA with a predetermined standard,

wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined standard is indicative of an age-related tissue disorder.

11. A method of determining the presence of a disorder characterized by accelerated or abnormal tissue aging in a patient, the method comprising the steps of;

(a) determining an amount of OP-1 protein present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 protein with a predetermined standard,

wherein a difference in the amount of OP-1 protein present in said sample and the predetermined standard is indicative of a disorder characterized by accelerated or abnormal tissue aging.

12. A method of determining the presence of a disorder characterized by accelerated or abnormal tissue aging in a patient, the method comprising the steps of;

(a) determining an amount of OP-1 mRNA present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 mRNA with a predetermined standard;

wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined standard is indicative of a disorder characterized by accelerated or abnormal tissue aging.

13. A method for determining the clinical severity of an age-related tissue disorder in a patient, the method comprising the steps of

(a) determining an amount of OP-1 protein present in a joint tissue sample; and

b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 protein present in joint tissue samples obtained from members of a population having said age-related tissue disorder with the clinical severity of said disorder,

thereby to determine the clinical severity of the age-related tissue disorder in said patient.

14. A method for determining the clinical severity of an age-related tissue disorder in a patient, the method comprising the steps of

(a) determining an amount of OP-1 mRNA present in a joint tissue sample; and

b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 mRNA present in joint tissue samples obtained from members of a population having said age-related tissue disorder with the clinical severity of said disorder,

thereby to determine the clinical severity of the age-related tissue disorder in said patient.

15. A method for determining the clinical severity of a disorder characterized by accelerated or abnormal tissue aging in a patient, the method comprising the steps of

(a) determining an amount of OP-1 protein present in a joint tissue sample; and

b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 protein present in joint tissue samples obtained from members of a population having said disorder with the clinical severity of said disorder,

thereby to determine the clinical severity of the disorder characterized by accelerated or abnormal tissue aging in said patient.

16. A method for determining the clinical severity of a disorder characterized by abnormal tissue aging in a patient, the method comprising the steps of

(a) determining an amount of OP-1 mRNA present in a joint tissue sample; and

b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 mRNA present in joint tissue samples obtained from members of a population having said disorder with the clinical severity of said disorder,

thereby to determine the clinical severity of the disorder characterized by abnormal tissue aging in said patient.

17. The method according to any one of claims 9-16, wherein the joint tissue sample comprises a tissue selected from the group consisting of cartilage, ligament, meniscus, tendon, synovium, synovial fluid, and intervertebral disc tissue.

18. The method according to any one of claims 9-16, wherein the joint tissue sample comprises synovial fluid.

19. The method according to any one of claims 9, 11, 13, or 15, wherein the step of determining an amount of OP-1 protein present in the joint tissue comprises performing an enzyme-linked immunosorbent assay (ELISA).

20. The method according to any one of claims 9, 10, 13 or 14, wherein the age-related tissue disorder is independent of chronological age.

21. The method according to any one of claims 9, 10, 13 or 14, wherein the age-related tissue disorder is indicative of a disease selected from the group consisting of osteoarthritis and osteoporosis.

22. The method according to any one of claims 11, 12, 15, or 16, wherein the disorder characterized by abnormal tissue aging is a degenerative diseases.

23. The method according to any one of claims 9, 10, 11, or 12, wherein the predetermined standard is age-correlated.

24. A method of determining the presence of an autoimmune disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 protein present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 protein with a predetermined standard;

wherein a difference in the amount of OP-1 protein present in said sample and the predetermined standard is indicative of the presence of an autoimmune disease.

25. A method of determining the presence of an autoimmune disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 mRNA present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 mRNA with a predetermined standard;

wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined standard is indicative of the presence of an autoimmune disease.

26. A method for determining the clinical severity of an autoimmune disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 protein present in a joint tissue sample; and

(b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 protein present in joint tissue samples

obtained from members of a population having said autoimmune disease with the clinical severity of said disease,

thereby to determine the clinical severity of the autoimmune disease in said patient.

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26. A method for determining the clinical severity of an autoimmune disease in a patient, the method comprising the steps of

(a) determining an amount of OP-1 mRNA present in a joint tissue sample; and

(b) applying to said amount a predetermined statistical relationship, said statistical relationship correlating a range of amounts of OP-1 mRNA present in joint tissue samples obtained from members of a population having said autoimmune disease with the clinical severity of said disease,

thereby to determine the clinical severity of the autoimmune disease in said patient.

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27. The method of any one of claims 23-26, wherein said autoimmune disease is associated with a histomorphological change in a joint tissue.

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28. The method of any one of claims 23-26, wherein the joint tissue sample comprises a tissue selected from the group consisting of cartilage, ligament, meniscus, tendon, synovium, synovial fluid, and intervertebral disc tissue.

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29. The method of any one of claims 23-26, wherein the joint tissue sample comprises synovial fluid.

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30. The method of claim 23 or 25, wherein the step of determining an amount of OP-1 protein present in the joint tissue sample comprises performing an enzyme-linked immunosorbent assay (ELISA).

32 24-27
31. The method of any one of claims 23-26, wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, lupus erythematosus and non-inflammatory monoarthritis, and psoriasis.

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32. The method of any one of claims 1, 2, 9, 10, 11, 12, 23 or 24, wherein the predetermined standard comprises a range of values.

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33. The method of claim 1, 2, 9, 10, 11, 12, 23 or 24, wherein the predetermined standard is an age-adjusted standard.

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34. A method of determining a predisposition for a disease which results in cartilage degradation or degeneration in a patient, the method comprising the steps of

(a) determining an amount of OP-1 protein present in a joint tissue sample from the patient; and

(b) comparing said amount of OP-1 protein with a predetermined standard;

wherein a difference in the amount of OP-1 protein present in said sample and the predetermined standard is indicative of a predisposition for the inflammatory disease, disorder characterized by abnormal tissue aging in a patient, autoimmune disease, joint degenerative disease, and/or joint trauma-induced disease.

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35. A method of determining the clinical status of a joint region of a patient, the method comprising the steps of:

(a) determining an amount of OP-1 protein present in a tissue sample obtained from a joint region of a patient;

(b) comparing said amount with a predetermined standard, thereby to determine a value representative of the deviation of said amount with said standard,

wherein said value is indicative of the clinical status of said joint region.

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36. A method according to claim 35, wherein said predetermined standard is correlated with the age of said patient and is representative of an amount of OP-1 protein expected to be present in a clinically-normal joint region.

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37. A method according to claim 35, wherein said predetermined standard comprises a range of values.

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38. A method of monitoring regenerative or degenerative activity within a joint region of a patient, the method comprising the steps of:

determining the relative amount of OP-1 protein present in at least one tissue sample obtained from the joint region of said patient, wherein the at least one said tissue sample corresponds to a point in time which is later than a first, earlier tissue sample for which OP-1 protein amounts are already determined,

wherein an increase in the amount of OP-1 protein present in said later tissue sample is indicative of an onset of, or increase in, regenerative activity in said joint region, and whereas a decrease in the amount of OP-1 protein present in said later tissue sample is indicative of a cessation of, or decrease in, regenerative activity in said joint region.

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39. A method of determining the clinical status of a joint region of a patient, the method comprising the steps of:

(a) determining an amount of OP-1 protein present in a tissue sample obtained from a joint region of a patient; and

(b) comparing said amount with a predetermined standard indicative of an amount of OP-1 protein expected to be present in a clinically normal joint region,

wherein an amount determined in step (a) that is about equal to said standard is indicative of a normal clinical status of said joint region of said patient, and an amount that is not about equal to said standard is indicative of an abnormal clinical status of said joint region of said patient.

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40. A method for determining the effective dose of an anti-inflammatory agent in a subject, the method comprising the steps of:

(a) obtaining a tissue, body fluid or cell sample from a subject to whom a dose of an anti-inflammatory agent is earlier administered ;

(b) determining OP-1protein concentration or OP-1 mRNA concentration in said sample;

(c) determining in said same sample the concentration of protein or mRNA encoded by a second gene whose expression is not altered by inflammation; and

(d) comparing the OP-1 protein or mRNA concentration to the protein or mRNA concentration of the second gene, wherein the difference between the OP-1 protein or mRNA concentration and the second gene protein or mRNA concentration is indicative of the effectiveness of the anti-inflammatory agent dose in the patient.

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~~41~~. A method for determining the ability of a patient to respond to an anti-inflammatory agent, the method comprising the steps of:

(a) obtaining a tissue, body fluid or cell sample from a subject to whom a dose of an anti-inflammatory agent was earlier administered;

(b) determining OP-1 protein concentration or OP-1 mRNA concentration in said sample;

(c) determining in said same sample the concentration of protein or mRNA encoded by a second gene whose expression is not altered by inflammation; and

(d) comparing the OP-1 protein or mRNA concentration to the protein or mRNA concentration of the second gene to create a ratio, wherein the subject is responsive to an anti-inflammatory agent if the ratio is higher than a predetermined control ratio for untreated or nonresponsive subjects, or similar to prior ratios for the subject when the subject was previously determined to be responsive.

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~~42~~. The method of any one of claims 1-4, wherein the inflammatory disease is rheumatoid arthritis.

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~~43~~. The method of any one of claims 9, 10, 13 or 14, wherein the age-related tissue disorder is osteoarthritis.

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~~44~~. The method of any one of claims ~~23~~-26, wherein the autoimmune disease is rheumatoid arthritis.

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48. A method of determining joint tissue deterioration, including deterioration associated with disease or age, the method comprising the steps of:

(a) determining in a joint tissue sample an amount of bone morphogenic protein related to OP-1 or an amount of mRNA encoding a protein related to OP-1; and

(b) comparing said amount of protein or mRNA with a predetermined standard;

wherein a difference in the amount of protein or mRNA in said sample and the predetermined standard is indicative of joint tissue deterioration.

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46. A method of determining joint tissue aging, including premature aging associated with disease, the method comprising the steps of:

(a) determining in a joint tissue sample an amount of bone morphogenic protein related to OP-1 or an amount of mRNA encoding a protein related to OP-1; and

(b) comparing said amount of protein or mRNA with a predetermined standard;

wherein a difference in the amount of protein or mRNA in said sample and the predetermined standard is indicative of joint tissue aging.